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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,593	01/21/2004	Lee-Hwei K. Sun	02SUN2001-A	3775

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EXAMINER	
DEBERRY, REGINA M	

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1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,593	SUN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *4-6,13,14 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-12,15 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 05 March 2007 has been entered in full. Claims 4-6, 13, 14, 16-19 are withdrawn. Claims 1-3, 7-12, 15 and 20 are under examination.

Withdrawn Objections And/Or Rejections

The objection to claims 9 and 20, as set forth at page 4 of the previous Office Action (26 May 2006), is *withdrawn* in view of the amendment (05 March 2007).

The rejection to claims 2, 3, 6, 7, 11, 12 and 14 under 35 U.S.C. 112, second paragraph, as set forth at pages 4-6 of the previous Office Action (26 May 2006), is *withdrawn* in view of the amendment (05 March 2007).

The rejection to claims 1, 2, 7, 8, 10, 11 and 20 under 35 U.S.C. 112, first paragraph, scope of enablement, as set forth at pages 6-8 of the previous Office Action (26 May 2006), is *withdrawn* in view of the amendment (05 March 2007).

Terminal Disclaimer

The terminal disclaimer (TD) entered 10 August 2006 was not accepted because the Ownership information is not complete.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-10 and 20 remain rejected under 35 U.S.C. 112, second paragraph. The basis for this rejection is set forth at pages 4-6 of the previous Office Action (26 May 2006).

Claims 8-10 are indefinite because the term "CHO-derived cell line" is unclear. It is suggested that the instant claims be amended to recite, "..CHO cell line transfected with DNA encoding the recombinant HuEPO-L-vFC fusion protein..."

Claim 20 is indefinite because it is unclear and lacks antecedent basis. It is suggested that claim 20 be amended to recite, "..**wherein said** method comprises.." instead of "..**which method** comprises.." (please see 2nd-3rd line) "..under conditions, **wherein the recombinant fusion protein**.." (please see 4th-5th line). It is suggested that the instant claim be amended to recite, "..purifying the expressed **recombinant fusion protein**.." (please see 6th line). Lastly, claim 20 still recites part of the Markush language "..selected from the group consisting of.." (Please see 12th-13th line). This recitation should be deleted.

NEW CLAIM REJECTIONS/OBJECTIONS

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 3, 9, 12 and 20 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 7 and 12, respectively of U.S. Patent No. US 6,900,292 B2. The basis for this rejection is set forth at pages 8-10 of the previous Office Action (15 June 2001).

Claim 3 of the instant application is drawn to the recombinant HuEPO-L-vFc fusion protein of claim 1 or claim 2, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 with Pro331Ser mutation of SEQ ID NO:18. Claim 3 depends from claim 1, which is drawn to a recombinant HuEPO-L-vFC fusion protein consisting of HuEPO, a peptide linker, and a human IgG Fc variant, wherein the recombinant HuEPO-L-vFc fusion protein exhibits *in vitro* biological activity similar to or higher than that of rHuEPO on a molar basis. Claim 1 of U.S. Patent No. US 6,900,292 B2 is drawn to a recombinant HuEPO-L-vFC fusion protein consisting of HuEPO, a peptide linker, and a human IgG Fc variant, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 with Pro331Ser mutation as SEQ ID NO:18. Claims 3 (application) and 1 (patent) are both drawn to a

recombinant HuEPO-L-vFc fusion protein consisting of HuEPO, a peptide linker and a human IgG Fc variant (SEQ ID NO:18).

Claim 9 of the instant application is drawn to a CHO-derived cell line producing the HuEPO-L-vFc fusion protein of claim 1, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 of SEQ ID NO:18 and the IgG Fc contains amino acid mutations to attenuate effector functions, a flexible peptide linker containing 20 or fewer amino acids is present between HuEPO and human IgG Fc variant. Claim 6 of U.S. Patent No. US 6,900,292 B2 is drawn to the CHO cell line transfected with DNA encoding the recombinant HuEPO-L-vFc fusion protein of claim 1, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 with Pro331Ser mutation as SEQ ID NO:18, the IgG Fc contains amino acid mutations to attenuate effector functions, a flexible peptide linker containing about 20 or fewer amino acids is present between HuEPO and human IgG Fc variant, and the HuEPO-L-vFc fusion protein exhibits an enhanced *in vitro* biological activity of at least 2 fold relative to that of rHuEPO on a molar basis. Claims 9 (application) and 6 (patent) are both drawn to a CHO cell line transfected with DNA encoding a recombinant HuEPO-L-vFc fusion protein consisting of HuEPO, a peptide linker and a human IgG Fc variant (SEQ ID NO:18).

Claims 12 and 20 of the instant application are drawn to methods of making a recombinant fusion protein comprising HuEPO, a flexible peptide linker, and a human IgG Fc variant, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 of SEQ ID NO:18. Claim 12 depends from claim 10, which is

drawn to a method for making a recombinant fusion protein comprising HuEPO, a flexible peptide linker, and a human IgG Fc variant. Claims 7 and 12 of U.S. Patent 6,900,292 B2 are drawn to methods of making a recombinant fusion protein comprising HuEPO, a flexible peptide linker, and a human IgG Fc variant, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 of SEQ ID NO:18. Claims 12 and 20 (application) and 7 and 12 (patent) are both drawn to methods of making a recombinant fusion protein comprising HuEPO, a flexible peptide linker, and a human IgG Fc variant, wherein the human IgG Fc variant comprises a hinge, CH2 and CH3 domains of human IgG2 of SEQ ID NO:18.

The rejection is maintained because the terminal disclaimer (TD) entered 10 August 2006 was not accepted.

Claim Rejections - 35 USC § 102(a)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 7, 8, 10, 11 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Cox *et al.*, WO 01/03737 (18 January 2001).

Cox *et al.* teach method of making fusion proteins comprising a growth factor fused to a peptide linker fused to an immunoglobulin domain (abstract and page 8, lines 13-18). Peptide linkers include a mixture of glycine and serine residues, such as SerGly

or Ser(GlyGlySer)n, wherein n can be 1-7. Preferred linkers are 1-50 amino acids in length (page 5, line 39-page 6, line 2; page 7, lines 27-34; page 9, lines 5-10 and page 22, lines 11-21). Examples of growth factors include EPO (page 6, lines 5-7, page 7, lines 5-26). Cox *et al.* teach variants in the Fc region (page 7, lines 35-38 and page 8, lines 13-18). Cox et al. teach that Fc fusion proteins prolong the circulating half-life of protein pharmaceuticals. Cox et al. teach that fusion proteins with high activity can produce greater therapeutic benefits at lower doses than fusion proteins with lower specific activity. Cox *et al.* teach the use of CHO cells to produce the fusion protein (page 9, lines 32-34). Cox et al. teach small and large-scale transfections and harvesting of COS cells (page 16, line 12-page 17, line 32).

Cox *et al.* do not explicitly teach that the EPO fusion protein exhibits *in vitro* biological activity similar to or higher than that of recombinant human EPO on a molar basis, or the microgram amounts of fusion protein produced in a CHO cell line transfected with said fusion protein. However, the prior art structure has all the features required to perform the activity recited in the instant claims. Furthermore, as there are no claimed distinguishing features between the fusion protein or manipulative differences in the method steps to patentably distinguish the claimed invention from the instant patent of Cox *et al.*, the biological activity would be an inherent feature of the product.

Claim Rejections - 35 USC § 102(e)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 7, 8, 10, 11 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Gillies et al., US Patent Application Publication US 2005/0202538 A1.

Gillies et al. teach EPO-Fc fusion proteins with improved pharmacokinetics, nucleic acids, cells and methods of making the fusion protein (abstract; para 0003). Gillies et al. teach variants in the Fc region (para 0009; 0013-0018 and para 0041-0049). Gillies et al. teach that the EPO portion is indirectly linked to the Fc. Gillies et al. teach that Fc-EPO fusion proteins have a prolong serum half-life and increased *in vivo* potency. The Fc-EPO fusion protein can include a linker between the Fc portion and the EPO portion (para 0040). The linker can generally contains between 1 and 25 amino acids. The linker contains an Asn-Ala-Thr amino acid sequence (para 0062). Gillies et al. teach that the fusion protein can be made in COS cells (para 0087). Gillies et al. teach that stable transfected cells are often preferred for large-scale production (para 0095-0098).

Gillies et al. do not explicitly teach that the EPO fusion protein exhibits *in vitro* biological activity similar to or higher than that of recombinant human EPO on a molar basis, or the microgram amounts of fusion protein produced in a CHO cell line transfected with said fusion protein. However, the prior art structure has all the features required to perform the activity recited in the instant claims. Furthermore, as there are

no claimed distinguishing features between the fusion protein or manipulative differences in the method steps to patentably distinguish the claimed invention from the instant patent of Gillies et al., the biological activity would be an inherent feature of the product.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
5/14/07

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5/17/07